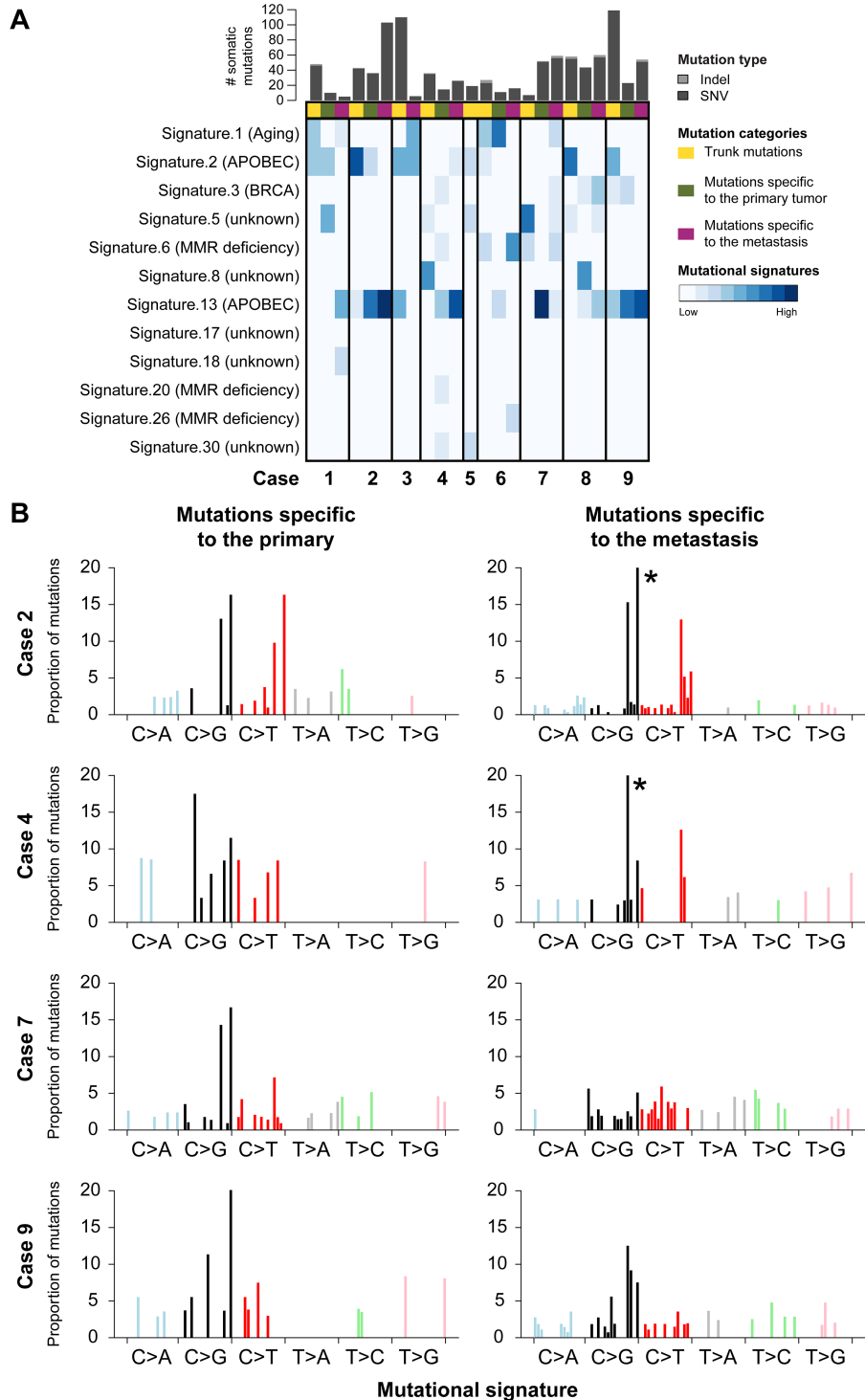


Supplementary Fig. S3



Supplementary Fig. S3: Evolution of mutational signatures in treatment-naïve patients with *de novo* synchronous metastatic breast cancer. (A) Heatmap represents the similarity of the observed mutational signatures (blue, see color key) to those previously observed in human cancers (15, 36), separately for the trunk mutations (yellow), the mutations specific to the primary tumor (green) and the mutations specific to the metastatic lesion (pink). **(B)** Barplots illustrate the mutational signatures of the mutations specific to the primary tumor and the metastatic lesion of Cases 2, 4, 7 and 9. In each panel, the colored barplot illustrates each mutational signature according to the 96 substitution classification defined by the substitution classes (C>A, C>G, C>T, T>A, T>C and T>G bins) and the 5' and 3' sequence context, normalized using the observed trinucleotide frequency in the human exome to that in the human genome. The bars are ordered first by mutation class (C>A/G>T, C>G/G>C, C>T/G>A, T>A/A>T, T>C/A>G, T>G/A >C), then by the 5' flanking base (A, C, G, T) and then by the 3' flanking base (A, C, G, T). *: >20%.